the difference in hfs's between **3a** and **3b** is unknown, it is not possible to conclude whether at low temperature only **3a**, **3b**, or a mixture of both is present.

It seems possible that cyclobutadiene radical cations substituted with oligomethylene chains of a different length or with additional substituents on the pentamethylene chain(s) can be studied in a similar way.

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Registry No. 1, 84960-18-9; 2, 84960-19-0; 3, 84960-20-3.

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Anodic α-Methoxylation of N-Carbomethoxylated or N-Acylated α-Amino Acid Esters and α-Amino β-Lactams[1]

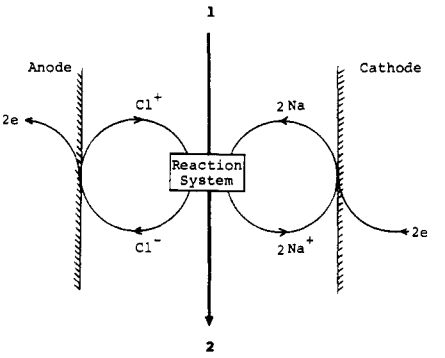
Summary: A new practical method of introducing a methoxyl group to the α-position of α-amino acid derivatives and α-amino β-lactams has been exploited by utilizing indirect electrochemical oxidation as a key reaction.

Sir: Since the discovery of 7α-methoxycephalosporins, potent antibiotics against Gram-negative bacteria,[2] much effort has been devoted to the development of new methods for introducing a methoxyl group to the 6-position of penicillins[3] or the 7-position of cephalosporins[4] and 1-oxacephems.[5] In general, the α-methoxylation of these β-lactams is the same type of reaction as the α-methoxylation[6] of α-amino acid esters. The α-methoxylated α-amino acids are also versatile reagents for amidoalkylation[6a-e] and useful intermediates leading to α,β-unsaturated α-amino acids.[6e-g]

Table I. Anodic α-Methoxylation[a] of 1b-e

run	1	supporting electrolyte MX (equiv)[b]	electricity passed, F/mol	yield of 2 (%)[c]
1	1b	NaCl (0.1)	10	2b (89)[d]
2	1b	NaCl (0.25)	10	2b (80)[e]
3	1b	NaCl (0.5)	10	2b (83)
4	1b	NaCl (1.0)	10	2b (70)[f]
5	1b	LiCl (0.5)	10	2b (76)
6	1b	KCl (0.5)	10	2b (78)
7	1b	Et_4NCl (0.5)	10	2b (90)
8	1b	NaBr (0.5)	10	2b (47)
9	1b	KI (0.5)	10	2b (0)[g]
10	1b	Et_4NOTs (0.1)	10	2b (6)[g]
11	1b	NaOAc (0.5)	10	2b (0)[g]
12	1c	NaCl (0.5)	10	2c (90)
13	1d	NaCl (0.5)	10	2d (91)
14	1e	NaCl (0.5)	31	2e (62)

[a] Platinum plates were used as electrodes. [b] The ratio of MX to 1. [c] Constant current; 0.3 A. [d] Constant current; 0.1 A. [e] Constant current; 0.2 A. [f] Constant current; 0.5 A. [g] Most of starting compound was recovered.



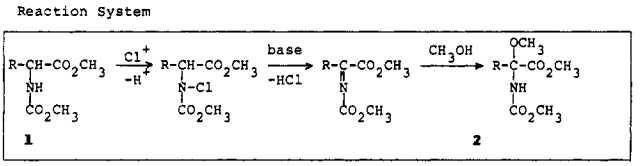
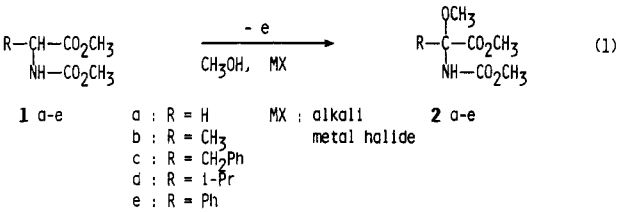


Figure 1. Schematic representation of the indirect α-methoxylation.

Thus, we have studied a new useful anodic α-methoxylation of α-amino acid derivatives **1** (eq 1), which is



(1)

applicable to the methoxylation of β-lactams. The yields of **2b** obtained under several conditions are summarized as runs 1-11 of Table I,[7] which also shows the results of the α-methoxylation of **1c-e** (runs 12-14). Also, it was found that this anodic α-methoxylation successfully worked in the α-methoxylation of lactams **3a,b** without cleavage of the β-lactam ring (eq 2).[7]

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(7) IR and NMR data and elemental analyses of products coincided with assigned structures.

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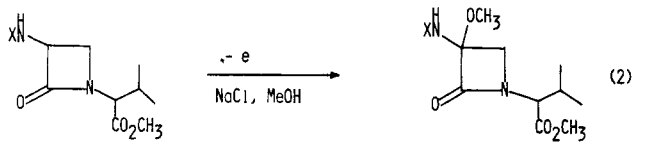
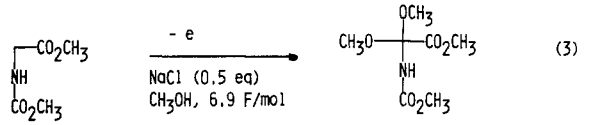


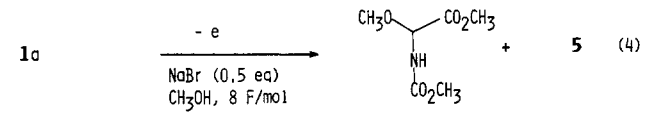
3a : X = CO_2CH_3 **4a** : 92 % (4.3 F/mol)
3b : X = CO_2CH_2Ph **4b** : 30 % (4.0 F/mol)

Although the oxidation of **1a** using NaCl resulted in the formation of α,α-dimethoxylated product (**5**) (eq 3),[7] the

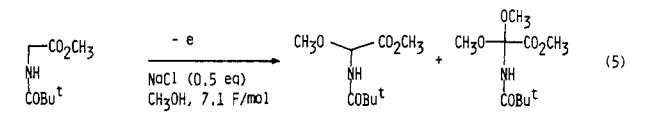


1a **5** 95 %

preparation of an α-monomethoxylated product (**2a** or **7**) could be accomplished by the use of NaBr (eq 4) or by changing the structure of the substrate from carbamate to bulky amide (**6**) (eq 5).[7]



2 66 % 26 %

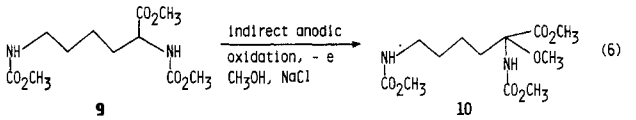


6 **7** 86 % **8** 11 %

The reaction conditions for this anodic α-methoxylation are simple and mild as exemplified below.

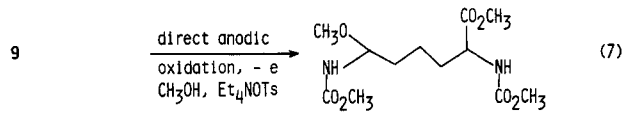
Into a cell equipped with platinum plate electrode (2 × 2 cm) was added a solution of *N*-(carbomethoxy)alanine methyl ester (**1b**) (4 mmol) in methanol (30 mL) containing sodium chloride (0.4 mmol). After a constant current of 0.1 A (terminal voltage 15 V) was passed through the solution for 10.8 h (10 F/mol of electricity) with external cooling in an ice–water bath, the solvent was removed in vacuo without heating and water was added to the residue. This mixture was extracted with CH_2Cl_2, and the extracts were dried with $MgSO_4$. Evaporation of CH_2Cl_2 gave *N*-(carbomethoxy)-α-methoxyalanine methyl ester (**2b**) as crystals (mp 94–95 °C) in 89% yield.

At least two mechanisms are conceivable for this α-methoxylation: (i) direct anodic oxidation of **1** and (ii) indirect oxidation of **1** with some oxidizing reagent anodically generated in situ. The anodic methoxylation of carbamates of aliphatic primary and secondary amines in methanol using tetraethylammonium *p*-toluenesulfonate (TEATS) as a supporting electrolyte has been shown[8] to proceed through the direct oxidation pathway. The transformation of **1b** to **2b**, however, was negligible under these conditions when using TEATS or sodium acetate as a supporting electrolyte (runs 10 and 11), whereas the methoxylation proceeded successfully in the presence of an alkali metal chloride or bromide. These facts suggest that **1** was oxidized indirectly by some active species such as Cl^+ (Br^+) or CH_3OCl (CH_3OBr)[9] that was generated by anodic oxidation of Cl^- (Br^-) in methanol. In fact, the anodic reaction of **9** in methanol containing NaCl gave selectively the α-methoxylated α-amino acid derivatives (**10**)[7] (eq 6), while the direct anodic methoxylation of **9** in



9 **10** 70 % (10 F/mol)

methanol containing TEATS took place at the position α to the ω-amino group, yielding only **11** (eq 7).[7]



11 51 % (12 F/mol)

Furthermore, Table I shows that the yields of **2b** are almost independent of the amount of NaCl (runs 1–4), suggesting that Cl^- is regenerated in the reaction system. Accordingly, a schematic diagram of this indirect α-methoxylation is shown in Figure 1, in which NaCl behaves as a mediator.[10]

The new methods reported in this paper are highly promising for the α-methoxylation of N-carbomethoxylated or N-acylated α-amino acid esters and α-amino β-lactams, since the reaction conditions are mild, operation is simple, and no oxidizing agents are necessary. The application of this method to more complicated β-lactams and free amino acids or esters is now in progress.

Registry No. **1a**, 70288-73-2; **1b**, 28819-00-3; **1c**, 41844-71-7; **1d**, 85235-39-8; **1e**, 85235-40-1; **2a**, 64356-73-6; **2b**, 85235-41-2; **2c**, 85235-42-3; **2d**, 85235-43-4; **2e**, 85235-44-5; **3a**, 85235-45-6; **3b**, 19789-85-6; **4a**, 85235-46-7; **4b**, 85235-47-8; **5**, 85235-48-9; **6**, 63974-28-7; **7**, 85235-49-0; **8**, 85235-50-3; **9**, 85235-51-4; **10**, 85235-52-5; **11**, 85235-53-6.

(8) For examples, see: (a) Shono, T.; Hamaguchi, H.; Matsumura, Y. *J. Am. Chem. Soc.* **1975**, *97*, 4264. (b) Shono, T.; Matsumura, Y.; Tsubata, K. *Ibid.* **1981**, *103*, 1172; (c) *Tetrahedron Lett.* **1981**, *22*, 2411; (d) *Ibid.* **1981**, *22*, 3249. (e) Shono, T.; Matsumura, Y.; Tsubataa, K.; Takata, J. *Chem. Lett.* **1981**, 1121.

(9) The oxidation of α-amino acid derivatives with *tert*-butyl hypochlorite has been known,[3] though this is not necessarily applicable for the large-scale preparation.

(10) For examples, see: (a) Shono, T.; Matsumura, Y.; Hayashi, J.; Mizoguchi, M. *Tetrahedron Lett.* **1979**, 165; (b) *Ibid.* **1979**, 3861; (c) *Ibid.* **1980**, *21*, 1867. (d) Shono, T.; Matsumura, Y.; Yamane, S.-i.; Kashimura, S.; *Chem. Lett.* **1982**, 565.

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Unusually Slow Thermal Isomerization of Alkyldihaloboranes. A Highly Regio- and Stereospecific Synthesis of Alkyldihaloboranes from Labile Olefinic Structures

Summary: The thermal isomerizations of 3-hexyldihaloboranes were systematically examined at 150 °C in *o*-dichlorobenzene. The 3-hexylboranes derived from the hydroboration of *cis*-3-hexene with $HBCl_2{\cdot}SMe_2$ and $HBBr_2{\cdot}SMe_2$ are exceptionally resistant to thermal isomerization, a discovery of considerable importance for the regio- and stereospecific synthesis of alkyldihaloborane intermediates from highly labile olefinic structures.

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